Zdiv corrected in response to notice to comply.txt SEQUENCE LISTING <110> YOUNG, ANDREW A. VINE, WILL BEELEY, NIGEL R.A. PRICKETT, KATHRYN S. <120> INOTROPIC AND DIURETIC EFFECTS OF GLP-1 AND GLP-1 AGONISTS <130> 256-152DIV US <140> 10/656,093 <141> 2003-09-05 <160> 75 <170> PatentIn Ver. 2.1 <210> 1 <211> 39 <212> PRT <213> Heloderma horridum <220> <223> Exendin-3 <400> 1 His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 10^{-15} Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser 20 25 30 Ser Gly Ala Pro Pro Pro Ser <210> 2 <211> 39 <212> PRT <213> неloderma suspectum <220> <223> Exendin-4 His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 10 15Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser $20 \hspace{1cm} 25 \hspace{1cm} 30$ Ser Gly Ala Pro Pro Pro Ser <210> 3 <211> 30 <212> PRT <213> Homo sapiens <220>

<223> GLP-1

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Revised 256-152div corrected in response to notice to comply.txt
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Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
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Revised 256-152div corrected in response to notice to comply.txt
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Revised 256-152div corrected in response to notice to comply.txt
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<223> provided no more than three of Xaa3, Xaa5, Xaa6, Xaa8,
       Xaa10, Xaa11, Xaa12, Xaa13, Xaa14, Xaa15, Xaa16, Xaa17,
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Revised 256-152div corrected in response to notice to comply.txt Xaa19, Xaa20, Xaa21, Xaa24, Xaa25, Xaa26, Xaa27 or Xaa28 are Ala; and the compound is not exendin-3 or exendin-4 <220> <223> this peptide may encompass 28-39 residues, wherein residues 1-28 are constant and residues 29-39 may vary in length according to the specification Xaa Xaa Xaa Xaa Xaa Xaa <210> 5 <211> 30 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Exendin or GLP-1 agonist <220> <223> C-term may be amidated His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 5 10 15Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly 20 25 30 <210> 6 <211> 28 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Exendin or GLP-1 agonist <220> <223> C-term amidated <400> 6 His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 5 10 15Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn 20 25 <210> 7 <211> 28 <212> PRT <213> Artificial Sequence

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Revised 256-152div corrected in response to notice to comply.txt
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
<210> 10
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<213> Artificial Sequence
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
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Revised 256-152div corrected in response to notice to comply.txt
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Revised 256-152div corrected in response to notice to comply.txt
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Revised 256-152div corrected in response to notice to comply.txt 5 \hspace{1cm} 10 \hspace{1cm} 15
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Revised 256-152div corrected in response to notice to comply.txt
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Revised 256-152div corrected in response to notice to comply.txt
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20 25 30
Ser Gly Ala Pro Pro Pro
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Revised 256-152div corrected in response to notice to comply.txt
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Ser Gly Ala Pro Pro Pro
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20 25 30
Ser Gly Ala Pro Pro
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Revised 256-152div corrected in response to notice to comply.txt
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20 25 30
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Revised 256-152div corrected in response to notice to comply.txt
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20 25 30
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<210> 46
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20 25
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Revised 256-152div corrected in response to notice to comply.txt
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30
Ser Gly Ala Xaa Xaa Xaa
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Revised 256-152div corrected in response to notice to comply.txt
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Ser Gly Ala Pro Pro
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Revised 256-152div corrected in response to notice to comply.txt
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      GLP-1 agonist
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<222> (36)..(37)
<223> hPro
<220>
<223> C-term amidated
<400> 51
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 	 5 	 10 	 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30
Ser Gly Ala Xaa Xaa
35
<210> 52
<211> 36
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<221> MOD_RES
<222> (31)
<223> hPro
<220>
<221> MOD_RES
<222> (36)
<223> hPro
<220>
<223> C-term amidated
<400> 52
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 5 10 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30
Ser Gly Ala Xaa
<210> 53
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Revised 256-152div corrected in response to notice to comply.txt
<211> 35
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<223> C-term amidated
<400> 53
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30
Ser Gly Ala
<210> 54
<211> 30
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
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<400> 54
His Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 	 5 	 10 	 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly
20 25 30
<210> 55
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<221> MOD_RES
<222> (6)
<223> Naphthylala
<220>
<223> C-term amidated
<400> 55
His Gly Glu Gly Thr Xaa Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu 1 	 5 	 10 	 15
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
<210> 56
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25
<210> 57 <211> 28
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<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<223> C-term amidated
<400> 57
His Gly Glu Gly Thr Phe Ser Thr Asp Leu Ser Lys Gln Met Glu Glu 1 5 15
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25
<210> 58
<211> 28
<212> PRT
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<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<223> C-term amidated
<400> 58
His Gly Glu Gly Thr Phe Thr Ser Glu Leu Ser Lys Gln Met Ala Glu
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25
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<210> 59
<211> 28
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<220>
<223> Description of Artificial Sequence: Exendin or
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<220>
<221> MOD_RES
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<223> pentylgly
<220>
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
<210> 60
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<212> PRT
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<220>
<221> MOD_RES
<222> (22)
<223> Naphthylala
<220>
<223> C-term amidated
<400> 60
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Glu Ala Val Arg Leu Xaa Ile Glu Phe Leu Lys Asn
<210> 61
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<221> MOD_RES
<222> (23)
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Revised 256-152div corrected in response to notice to comply.txt
<223> tButylgly
<220>
<223> C-term amidated
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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
Glu Ala Val Arg Leu Phe Xaa Glu Trp Leu Lys Asn
20 25
<210> 62
<211> 28
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<223> C-term amidated
<400> 62
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
                                      10
Glu Ala Val Arg Leu Phe Ile Asp Phe Leu Lys Asn
<210> 63
<211> 33
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
      GLP-1 agonist
<220>
<223> C-term amidated
<400> 63
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu
Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
Ser
<210> 64
<211> 29
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Exendin or
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GLP-1 agonist
<220>
<223> C-term amidated
<400> 64
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly 20 25
<210> 65
<211> 37
<212> PRT
<213> Artificial Sequence
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      GLP-1 agonist
<220>
<221> MOD_RES
<222> (31)
<223> hPro
<220>
<221> MOD_RES
<222> (36)..(37)
<223> hPro
<220>
<223> C-term amidated
<400> 65
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu
Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser 20 25 30
Ser Gly Ala Xaa Xaa
<210>
       66
       29
<211>
<212>
       PRT
<213>
       artificial sequence
<220>
<223>
      Agonist of GLP-1
<220>
       MOD_RES
<221>
<222>
       (1)...(1)
       Ala is modified with an R group which can be 4-imidazopropionyl
       (des-amino-histidyl), 4-imidazoacetyl, or 4-imidazo-a,
       adimethyl-acetyl
<220>
```

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Revised 256-152div corrected in response to notice to comply.txt
       MOD_RES
<221>
<222>
       (19)..(19)
<223>
       Xaa is a Lys or Arg
<220>
<221>
       misc_feature
<222>
       (19)..(19)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       MOD_RES
<222>
       (27)..(27)
<223>
       Lys is modified with an R group consisting of C6 -C10 unbranched
       acyl, or is absent
<220>
<221>
<222>
       MOD_RES
       (29)..(29)
       Arg is modified with an R group consisting of Gly-OH or NH2
<223>
<400>
Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln
Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
<210>
       67
<211>
       19
<212>
       PRT
       artifical sequence
<213>
<220>
<221>
       MOD_RES
<222>
       (1)..(1)
<223>
       Ser is modified by H2N, H2N-Ser, H2N-Val-Ser, H2N-Asp-Val-Ser. or
       any one of SEQ ID NO:68 to 74
<220>
<221>
<222>
       MOD_RES
       (17)...(17)
<223>
       Xaa is a Lys or Arg
<220>
<221>
       misc_feature
<222>
       (17)..(17)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       MOD_RES
<222>
       (19)..(19)
<223>
       Arg can be modified by the group consisting of NH2, OH, Gly-NH2,
       or Gly-OH
<400>
Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
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Revised 256-152div corrected in response to notice to comply.txt
Xaa Gly Arg
<210>
       68
<211> 4
<212> PRT
<213> artificial sequence
<220>
      variable sequence insert for artificial GLP-1 analog
<223>
       68
<400>
Ser Asp Val Ser
<210> 69
<211>
      5
<212> PRT
<213> artificial sequence
<220>
<223> variable sequence insert for artificial GLP-1 analog
<400>
       69
Thr Ser Asp Val Ser
<210> 70
<211>
       6
<212> PRT
<213> artificial sequence
<220>
<223> variable sequence insert for artificial GLP-1 analog
<400> 70
Phe Thr Ser Asp Val Ser 1
<210> 71
<211> 7
<212> PRT
<213> artificial sequence
<223>
      variable sequence insert for artificial GLP-1 analog
<400> 71
Thr Phe Thr Ser Asp Val Ser
<210> 72
<211> 8
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Revised 256-152div corrected in response to notice to comply.txt
<212>
       PRT
<213>
       artificial sequence
<220>
       variable sequence insert for artificial GLP-1 analog
<223>
<400>
      72
Gly Thr Phe Thr Ser Asp Val Ser 1
      73
<210>
<211>
<212>
      PRT
<213> artificial sequence
<220>
      variable sequence insert for artificial GLP-1 analog
<223>
<400> 73
Glu Gly Thr Phe Thr Ser Asp Val Ser
<210>
      74
<211>
      10
<212> PRT
<213> artificial sequence
<220>
       variable sequence insert for artificial GLP-1 analog
<223>
<400> 74
Ala Glu Gly Thr Phe Thr Ser Asp Val Ser
       75
29
<210>
<211>
<212>
      PRT
<213>
       artificial sequence
<220>
<223>
       artificial
<220>
<221>
<222>
       MOD_RES
       (1)..(1)
<223>
       neurtal amino acid or D or N-acylated or alkylated form of
       histidine can be substituted for His
<220>
<221>
       MOD_RES
       (2)..(2) small neutral amino acid can be substituted for Ala
<222>
<223>
<220>
<221> MOD_RES
<222> (3)..(3)
```

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Revised 256-152div corrected in response to notice to comply.txt
<223> acidic or neutral amino acid can be substituted for Glu
<220>
       MOD_RES
<221>
<222>
       (4)..(4)
<223>
       neutral amino acid can be substituted for Gly
<220>
<221>
       MOD_RES
<222>
       (9)..(9)
       acidic amino acid can be substituted for Asp
<223>
<220>
<221>
      MOD_RES
<222>
       (10)..(10)
       Tyr can be substituted for Val
<223>
<220>
<221>
       MOD_RES
<222>
       (12)..(12)
<223> Lys can be substituted for Ser
<220>
<221>
<222>
      MOD_RES
       (15)..(15)
       Asp can be substituted for Glu
<223>
<220>
<221>
       MOD_RES
<222>
       (16)..(16)
<223>
       Ser can be substituted for Gly
<220>
<221>
<222>
       MOD_RES
       (17)..(17)
<223>
      Arg can be substituted for Gln
<220>
<221>
       MOD_RES
<222>
       (18)..(18)
       Arg can be substituted for Ala
<223>
<220>
<221>
       MOD_RES
<222>
       (20)..(20)
      Lys can be substituted for a neutral amino acid, arg, or a D form of lys
<223>
<220>
<221>
<222>
       MOD_RES
       (20)..(20)
<223>
       Gln can be substituted for Lys
<220>
<221>
       MOD_RES
<222>
       (25)..(25)
       Trp can be substituted for an oxidation-resistant amino acid
<223>
<220>
<221>
       MOD_RES
<222>
       (28)..(28)
       Lys can be substituted for a neutral amino acid, arg, or a D form
<223>
       of lys
                                        Page 30
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<220>
<221> MOD_RES
<222> (29)..(29)
<223> Xaa is a Gly, Gly-Arg, Gly-Arg-Gly, or absent

<220>
<221> misc_feature
<222> (29)..(29)
<223> Xaa can be any naturally occurring amino acid
<400> 75

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa
20 25
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